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Case Report

Neonatology Section

Scrub Typhus in a New Born

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ABSTRACT

Scrub typhus is an acute febrile mite-born rickettsial infection caused by *Orientia tsutsugamushi* (formely called *Rickettsia tsutsugamushi).* This infection is very uncommon in neonates. We report a case of 19-day-old newborn presenting with clinical features mimicking severe sepsis but was subsequently diagnosed with primary scrub typhus infection. The timely treatment resulted in dramatic response and complete recovery.

Keywords: Antenatal, Cytomegalovirus, *Rickettsia*, Sepsis, Trombiculid mites

CASE REPORT

A 19-day-old male infant was admitted in Neonatal Intensive Care Unit of our hospital with history of high grade fever, abdominal distension and difficulty in breathing since last three days and decreased oral acceptance, vomiting and loose stools for one day. He was delivered at a private hospital in Delhi through normal vaginal delivery with a birth weight of 3 kg. The antenatal and intrapartum periods were uneventful. He was discharged on second day of life and was exclusively breast fed before the illness.

At admission, the baby was febrile and irritable, had pallor with hepatosplenomegaly (liver 5 cm and spleen 3 cm below the costal margins) and few ecchymotic rashes present over abdomen and thighs. His weight was 3.2 kg at admission. The axillary temperature was 38°C, heart rate was 170/min, respiratory rate was 66/min and capillary refill time was less than three seconds.

A provisional diagnosis of late onset sepsis with meningitis was made and he was started on intravenous antibiotics and supportive measures to control fever and maintain adequate perfusion.

Investigations revealed anaemia (Hb 9.3 gm/dL), leukocytosis (26,000/mm^3 with 60% neutrophils) and thrombocyptopenia (platelet count- 30,000/mm^3). C-reactive protein (100 mg/dL, normal value less than 10 mg/dL) and pro-calcitonin (45 ng/mL, normal value less than 0.2 ng/mL) were highly positive. Kidney function tests were normal. Liver function tests revealed elevation of transaminases (aspartate transaminase and alanine transaminase of 110 and 90 IU/dL respectively). Cerebrospinal Fluid (CSF) examination showed aseptic meningitis (total cell count of 25 cells, with 90% lymphocytes, protein of 120 mg/L and sugar of 60mg/L with sterile culture). The blood (both BACTEC and fungal) cultures showed no growth. Dengue and malaria were ruled out by NS1 (Non-Structural Protein 1) antigen and rapid malarial antigen test and peripheral smear examination. IgM antibody for TORCH (Toxoplasmosis, Other agents, Rubella, Cytomegalovirus and Herpes Simplex) group of infections and VDRL (Venereal Disease Research Laboratory) test for syphilis were negative in both the mother and the neonate.

On fourth day of admission, due to deteriorating clinical status and development of respiratory distress and shock, the infant was mechanically ventilated and given inotropic support. Packed red blood cell transfusion and platelet concentrate were administered. The antibiotics were upgraded. The chest radiograph revealed presence of bilateral pleural effusions and ultrasound of abdomen revealed ascites. Both pleural and ascitic fluid examination were normal and cultures were sterile. Bone marrow examination was also done to rule out infiltrative and neoplastic disorders. Repeat blood, CSF and bone marrow cultures were sterile. The infant, however, continued to have high grade fever, hepatosplenomegaly, anasarca and persistent thrombocytopenia.

On 10th day of admission, we reevaluated the history provided by the family and it was revealed that some relatives from Assam had visited them a week before the onset of illness in the neonate. This prompted us to consider some unusual infection in the patient. We sent the rickettsial serology by card test (IgM ELISA) and it came positive for scrub typhus. The diagnosis was confirmed by PCR (Polymerase Chain Reaction) for eubacterial genome for *Orienta tsutsugamushi.* The mother was also investigated to rule out transplacental transfer of infection; however, both the investigations were negative in the mother.

Intravenous injection clarithromycin (15 mg/kg/day in two divided doses) was initiated in the patient. There was defervescence of fever with clinical improvement within 48 hours. Ventilatory and inotropic support was tapered and withdrawn over next two days. The body cavity effusions started resolving and there was regression in liver and spleen size. The platelet counts also normalised over one week. The antimicrobial was given for a total duration of 10 days. At the time of discharge, the infant had recovered fully and was on exclusive breast feeds.

DISCUSSION

Scrub typhus is most prevalent human rickettsial infection caused by *Orientia tsutsugamushi* transmitted by the bite of an infected mite chigger. It has been observed to be an important emerging infection in Northern India. It is now being increasingly reported from many parts of India including Maharashtra, Tamil Nadu, Kerala, Karnataka, Uttaranchal, Assam, Jammu and Kashmir, Himachal Pradesh, West Bengal and Rajasthan, highlighting its endemicity.

Orienta tsutsugamushi survives in the wild involving trombiculid mites (principal vectors) and other vertebrates (small mammals and birds), humans being the accidental hosts [1]. The infection is usually seen in people who come in contact with vector chiggers due to their occupational activities and in those who live in wide range of vegetation type from scrubs (terrain between woods and clearings), primary forests to gardens and beaches [2]. Scrub typhus infection has been rarely reported in the neonatal period [3,4].

The organism enters the human body and targets endothelial and reticulo-endothelial cells, leading to diffuse vasculitis and periva-sculitis. Vasculitis has been implicated to be the basic pathogenetic

mechanism responsible for skin rash, microvascular leakage, oedema, tissue hypoperfusion and end-organ ischemic injury. Widespread tissue hypoxic-ischemic insult can result in multi-organ dysfunction leading to high incidence of morbidity and mortality in untreated cases [5,6].

The incubation period of *Orienta tsutsugamushi* is 10-21 days in humans. The clinical manifestations may vary from mild undifferentiated fever to a severely potentially fatal disease leading to Multi Organ Dysfunction Syndrome (MODS).

The presentation of scrub typhus in children is non-specific and hence requires high index of suspicion for timely diagnosis. Due to wide variation in clinical presentation, the diagnosis of scrub typhus is often missed or diagnosed late.

The data regarding varied presentations in children is limited. In a study on children in Thailand suffering from scrub typhus infection, the most common signs observed were eschar at the site of bite, maculopapular rash, lymphadenopathy and hepatosplenomegaly [7].

Sankhyan N et al., in their study to describe the clinical profile of scrub typhus in children, found fever, hepatosplenomegaly, rash and oedema as the common clinical presentations followed by eschar at entry site, hypotension and multisystem involvement. Thrombocytopenia was observed in all the patients [8].

The clinical manifestations of scrub typhus in neonates remain unexplored, perhaps due to low clinical suspicion and overlapping signs and symptoms in this age group.

Our case was a 19-day-old neonate who presented with features suggestive of severe sepsis. He did not respond to standard management protocol for sepsis and all the investigations including blood and CSF cultures were sterile. This prompted us to investigate him for unusual infections at this age. After ruling out vector-borne diseases like dengue and malaria and congenital infections (TORCH), we sent the serology (IgM ELISA) for scrub typhus which came out to be positive and was confirmed by eugenome PCR-based test.

Scrub typhus has not been widely reported in neonatal period. Wang CL et al., reported a 26-day-old neonate presenting with vertically transmitted scrub typhus [3]. In our case, however, the mother was negative for both IgM antibodies and eubacterial genome for *O. tsutsugamushi*. Hence, in our case the infection was not vertically transmitted.

There is another case of primary scrub typhus infection in a 27-day old neonate, reported from Southern India, who presented with Multi Organ Dysfunction and responded to doxycycline [4]. Our patient also presented with MODS and recovered completely in response to intravenous injection clarithromycin. In both the cases, high index of suspicion, timely diagnosis and institution of early treatment saved the neonate from a life threatening infection.

Tetracycline or doxycycline and chloramphenicol remain the recommended treatment for scrub typhus [9]. Alternate drugs include rifampicin, roxithromycin and azithromycin [10,11]. We administered intravenous injectable clarithromycin due to hemodynamic unstability and inability to administer the antibiotic through oral route. Further, there is limited data on safety of other groups of antibiotic in neonates. The neonate showed remarkable improvement shortly after initiating the therapy.

Since, there is sparse literature on the clinical presentation of scrub typhus in neonates, a low threshold for suspecting this infection is warranted. There is often a delay in diagnosis due to non-specific clinical presentation mimicking neonatal sepsis and absence of widely available sensitive and specific diagnostic tests, which all contributes to significant morbidity and mortality. Timely diagnosis and early institution of appropriate antimicrobial treatment is often successful.

CONCLUSION

Our case highlights that a neonate presenting with fever, respiratory distress, organomegaly, oedema, thrombocytopenia and shock and showing no evidence of sepsis or congenital infections should always be investigated for scrub typhus especially in endemic regions of the country. The diagnosis is essential as the infection is treatable with antibiotics and if untreated can lead to MODS and mortality.

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